Remarks

Applicants have petitioned for reconsideration of the restriction requirement mailed on July 1, 2003. This Petition was mailed on October 1, 2003.

Claims 1-20, 23-34, 36, 37, and 39-49 are pending. Claims 2 and 3 have been amended. Claims 39-49 have been added. Support for the amendment to claims 2 and 3 can be found, for example, at page 10 of the specification (wherein the metastatic potential of a tumor is associated with elevated Pax 2 levels; comparing known cancerous or metastatic prostate cells with known non-cancerous or non-metastatic prostate cells); and page 9 (wherein levels of Pax 2 may be exploited diagnostically). Replacement sheets for drawings "5A3" and "5B" are provided ("11/14" and "12/14", respectively). Figures 5A3 and 5B are now properly and consecutively listed. Figure 5A3 was amended to insert "B1" and "B2", in order to clarify what is being described in the description of the drawings.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-9 and 15-16 were rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Examiner has supported her allegations of unpredictability of the state of the art by citing Gray *et al.* ("Gray"; 1995, *Cancer Research* 55:4800-4803). The applicants respectfully remind the Examiner that the present application demonstrates the correlation of Pax 2 expression with the progression of prostate cancer. The present application does not claim that Pax 2 expression will be identifiable in all prostate cancers, but provides evidence that suggests

Pax 2 expression is low or undetectable in normal prostatic cells or in benign prostatic hyperplasia. Gray examines chromosomal deletions rather than gene expression, and describes a different set of experiments, using a different experimental system. Thus, although Gray mentions prostate cancer, it cannot be used to demonstrate the unpredictability of the present invention as it refers to a distinct technical field.

The applicants respectfully submit that the present disclosure enables a person of ordinary skill in the art to use the claimed methods to detect Pax 2 mRNA in prostate tissue, urine, semen, blood or lymphatic circulation without undue experimentation. Pages 12-15 of the specification clearly teach methods capable of detecting Pax 2 in prostate tissue, urine, semen, blood or lymphatic circulation. The specification additionally states that prostate cells are shed into the urine (page 13, that cells derived from the prostate are found in small numbers in the urine and in the blood (pages 11-12) and suggests a FACS-based approach for enrichment of prostate cells from blood, semen and lymphatic circulation or urine samples (page 12). Furthermore, a method of interpreting data obtained from samples containing more than one cell type is provided. The specification also states that it will be appreciated that the methods of the invention may be performed on one or more individual cells, indicating that samples need not contain high cell numbers in order to be analyzed successfully.

The claims, as amended above, are directed to methods of monitoring the progression of prostate cancer, particularly the metastatic potential of a tumor that is thought to be associated with elevated Pax 2 levels (wherein normal cells and benign prostatic hyperplasias have low or undetectable amounts of Pax 2; and high or detectable amounts of Pax 2 are associated with

invasive prostate cancer; see specification throughout). In addition, Pax 2 expression may be utilized as a marker for the recurrence of prostate cancer in patients in remission (for example, see page 15 of the present specification).

Claim 3 is related to the identification of the presence and metastatic potential of prostate cancer. This is in accordance with the description that indicates that Pax 2 levels may be correlated with the development of prostate cancer, particularly during progression from benign prostatic hyperplasia to invasive prostate cancer (for example, see page 10, line 8, and pages 62-64).

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 1-9 and 15-16 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The applicants have deleted the term "level" from certain claims as pending. The applicants consider the foregoing amendments to moot the Examiner's objection to the term "level" as previously used in these claims. The applicants respectfully submit that one of ordinary skill in the art would understand the meaning of the term "level" in each of claims 10, 11, 14, 17, and 23. This term is used to further clarify the type of measurement used (i.e. "amount", "quantity", or "sum" of the protein present).

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AMENDMENT AND RESPONSE TO OFFICE ACTION

Allowance of claims 1-20, 23-34, 36, 37, and 39-49 is respectfully solicited.

Respectfully submitted,

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Certificate of Facsimile Transmission

I hereby certify that this Amendment and Response to Office Action, and any documents referred to as attached therein are being facsimile transmitted on this date, November 1, 2003, to the Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450.

Peggy Bailey

Date: October 31, 2003

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